Assessment of D-Dimer and Protein S in Egyptian Cirrhotic Patients with and without Ascites

Thesis

Submitted for partial fulfillment of the Master degree
in Internal Medicine

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2018

Acknowledgments

First and forever, thanks to ***Allah****, Almighty for giving me the strength and faith to complete my thesis and for everything else.*

All thanks to the soul of my Late ***Professor/ Mohamed Abd El-Ma'boud,*** *former Director of El-Demerdash Hospitals, Ain Shams University, may Allah give him mercy and acceptance in His Ferdous.*

I would like to express my deepest gratitude and appreciation to ***Prof. Dr. Wesam Ahmed Ibrahim,*** *Professor of Internal Medicine & Gastroenterology Faculty of Medicine – Ain Shams University, for her generous support and guidance to help me to put this work in its best form and for being an ideal model of a professor to follow. It was indeed an honor to work under her supervision.*

It is my pleasure to express my unlimited gratitude and deepest thanks to ***Dr. Mohamed Magdy Salama,*** *Lecturer of Internal Medicine & Gastroenterology, Faculty of Medicine – Ain Shams University, for his kind assistance, faithful supervision, precious help, valuable advice and guidance he offered me to complete this study. No words of gratitude can equal his help and support.*

I can't forget to thank with all appreciation ***Dr. Nesma Ahmed Safwat,*** *Lecturer of Clinical and Chemical Pathology Faculty of Medicine – Ain Shams University, for the efforts and time she has devoted to accomplish this work.*

I feel greatly indebted to all members of my family, specially my Parents and my Wife, without their great effort, encouragement, help and support this work could not become.

Millimi Adoum Djibrine

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LIST OF ABREVIATIONS

ADP	**:**	Adenosine diphosphate.
AICF	**:**	Accelerated intravascular coagulation and fibrinolysis.
ALT	**:**	Alanine aminotransferase.
ANOVA	**:**	A one-way analysis of variant.
AP	**:**	Antiplasmin.
APC	**:**	Activated protein C.
APTT	**:**	Activated partial thromboplastin time.
Arg	**:**	Arginine.
AST	**:**	Aspartate aminotransferase.
AT	**:**	Antithrombin.
BCE	**:**	Before common Era.
Ca	**:**	Calcium ions.
CLSI	**:**	Clinical and laboratory standards institute.
DIC	**:**	Disseminated intravascular coagulation.
DVT	**:**	Deep vein thrombosis.
EDTA	**:**	Ethylene Diamine Tetraacetic acid.
EGF	**:**	Endotholial growth factor.
Factor VIII:C	**:**	Factor coagulant activity.
Fig	**:**	Figure.
EPI	**:**	Extrinsic pathway inhibitor.
FDPs	**:**	Fibrin degradation products.
FEU	**:**	Fibrinogen equivalent units.
FFP	**:**	Fresh frozen plasma.
FSP	**:**	Fibrin Split Products.
GAGs	**:**	Glycosaminoglycans.
Gla	**:**	Glutamic acid.
GP	**:**	Glycoprotein.
HB	**:**	Hemoglobin.
HCC	**:**	Hepatocellular carcinoma.
HMWK	**:**	High molecular weight kininogen.

INR	**:**	International Normalized Ratio.
IVC	**:**	Inferior vena cava.
KDa	**:**	Kilodalton.
LSD	**:**	Least significant difference.
LVT	**:**	Liver function tests.
Ki	**:**	Power, energy
MELD	**:**	Model for end –stage liver disease.
mRNA	**:**	Messenger Ribonucleic acid.
MTHR	**:**	Methyltetrahydrofolate reductase.
MW	**:**	Molecular weight.
NASH	**:**	Non-alcoholic steato-hepatitis.
NPV	**:**	Negative predictive value.
OLT	**:**	Orthotopic liver transplantation.
PAI	**:**	Plasminogen activator inhibitor.
PAT-1	**:**	Plasminogen activator type1.
PBC	**:**	Primary biliary cirrhosis.
PDGF	**:**	Platelet – derived growth factor.
PPV	**:**	Positive predictive value.
PT	**:**	Prothrombin time.
PTT	**:**	Partial thromboplastin time.
P-value	**:**	Probability Value.
PVT	**:**	Portal vein thrombosis.
PZI	**:**	Protein Z dependant protease inhibitor.
r	**:**	Pearson's correlation coefficient.
RBCs	**:**	Red blood cells.
ROC	**:**	Receiver operating characteristic analysis.
RPM	**:**	Rotation per minute.
rFVIIa	**:**	Recombinant activated factor VII.
RVV	**:**	Venoum of vipera russelli.
SAAG	**:**	Serum ascites albumin gradient.
SBP	**:**	Spontaneous bacterial peritonitis.
SD	**:**	Standard deviation.
SEN	**:**	Sensitivity.

SHBG	**:**	Sex hormone binding globulin.
SPE	**:**	Specificity.
SPSS	**:**	Satistical program for social science.
TAFI	**:**	Thrombin activatable fibrinolysis inhibitor.
TEG	**:**	Thromboelastography.
TF	**:**	Tissue factor.
TFPI	**:**	Tissue factor pathway inhibitor.
TGF	**:**	Tumour growth factor.
t-PA	**:**	Tissue plasminogen activator.
TPO	**:**	Thrombopoitein.
TSR	**:**	Thrombin sensitive region.
TWBCs	**:**	Total white blood cells.
TXA2	**:**	Thromboxane A2.
U/S	**:**	Ultrasound.
u-PA	**:**	urokinase plasminogen activator.
VEGF	**:**	Vascular endothelial growth factor.
VT	**:**	Venous thromboembolism.
Viz	**:**	Namely, that is to say, as follows
vWF	**:**	Von Willebrand factor.

ABSTRACT

Background: The aim of this study was to evaluate the D-Dimer and Protein S in cirrhotic patients with and without ascites.

Methods: Patients with cirrhosis, who were admitted to hospital with decompensation of the liver (as defined by Development of ascites, hepatic encephalopathy) with and without ascites and underwent abdominal-sonography were included in this study. Compensated cirrhotic patients were also included. Laboratory data for computing Child-Pugh classification score, serum albumin, serum bilirubin, international normalized ratio, prothrombin time, transaminases, serum D-Dimer, and serum protein S, complete blood picture were collected for every patient. We tabulated hemostatic concentrations, liver functions tests, and sonogrophy parameters. WE analysed the correlation between D-Dimer, Protein S and each of the individual prognostic scores.

Results: A total of 90 patients with a diagnosis of liver cirrhosis were included in this study in wich 52 have no ascites, 38 patients were found to have ascites. In our study population with liver cirrhosis, we found statistically significance inverse correlations between D-Dimer and liver severity according to child-classification, also between D-Dimer and Protein S, As well as Protein S correlate with liver cirrhosis progression . However, the presence of ascites has and excess effects in occurrence of this two proteins (D-Dimer and protein S).

Conclusion: We observed the inverse relationship between D-Dimer and protein S, and statistically high significance inverse correlations between D-Dimer and liver severity according to Child-Pugh class used in this study among patients with liver cirrhosis, protein S correlate with liver damage severity positively. Although ascites have an additional excess impact on both proteins.

Keywords: Child-pugh classification; Cirrhosis; Ascites; D-Dimer; protein S.

Introduction

The liver plays a vital role in the coagulation process as it synthesizes and metabolizes the majority of fibrinolytic factors, as well as coagulation factors and inhibitors ***(Zhang et al., 2013).***

Advanced liver disease is commonly associated with complex hemostatic defects that include impaired synthesis of clotting factors and coagulation inhibitors in association with thrombocytopenia and platelets defects; in addition, liver cirrhosis is often accompanied by hyperfibrinolysis ***(Saray et al., 2012).***

Hemostasis is a dynamic balance between procoagulant and anticoagulant forces, the anticoagulant forces include two predominant classes of proteins, antithrombotic and fibrinolytic, whereas the antithrombotic proteins prevent fibrin clot formation, the fibrinolytic proteins lead to digestion of fibrinogen ***(Spadaro et al., 2008).***

D-dimer, a breakdown product of cross-linked fibrin, is a marker of ongoing fibrin turnover and represent an accurate marker of fibinolytic activity ***(Pabinger and Ay, 2009).***

Elevated plasma values of D-dimer are frequently found in patients with liver cirrhosis with a higher incidence

in decompensated disease. the underlying pathogenesis is still unclear and controversy still exist whether it is a primary phenomenon or induced secondary to coagulation activation and delayed hepatic clearance ***(Agarwal et al., 2000).***

The plasma glycoprotein protein S is mainly synthesized in the liver and is present in platelet a-granules and vascular endothelial cells, Protein S acts as an important cofactor for activated protein C (an anticoagulant) and enhances the protein C-mediated inactivation of factor Va and factor VIIIa ***(Zhang et al., 2013).***

Concentrations of protein S decline with deteriorating liver function, but this is not well documented in patients with cirrhosis ***(Zocco et al., 2009).***

On the basis of these findings we approve that in liver cirrhosis ascites counts to be the main factor associated with increased fibrinolytic activity and the underlying mechanism for these observation remains to be clarified ***(Saray et al., 2012).***

Aim of the Work

The aim of this study is to evaluate plasma levels of D-dimer and protein S in cirrhotic patients with and without ascites.